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IFW

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Annaliesa S. Anderson, <i>et al.</i>		
Serial No.:	10/564,458	Case No.:	21569YP
Filed:	January 12, 2006		
For:	POLYPEPTIDES FOR INDUCING A PROTECTIVE IMMUNE RESPONSE AGAINST STAPHYLOCOCCUS AUREUS		

Art Unit:
1645

Examiner:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COMMUNICATION

Sir:

Enclosed please find copies of the PCT Search Report and Written Opinion for the PCT application corresponding to the above-referenced application.

Respectfully submitted,

By Sh O

Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicant(s)

Merck & Co., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-1958

37 C.F.R. 1.8 Certificate of Mailing

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria VA 22313-1450, on the date appearing below.

MERCK & CO., INC.

By Sh O

Date October 16, 2006

Sheldon O. Heber

PATENT COOPERATION TREATY

PATENT DEPARTMENT

From the INTERNATIONAL SEARCHING AUTHORITY

SEP 25 2006

PCT

To:
MERCK & CO., INC.
126 EAST PENNSOLN AVENUE
RAHWAY, NJ 07065-0907

DOCKETED
SEP 22 2006
KATHY KLUTKOWSKI

REG. COORD.
DOCKET
ATTORNEY
MAINTENANCE
CASE REFERENCE
OTHER

S.O. HEBER

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

20 SEP 2006

Applicant's or agent's file reference
PCT 21569Y

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US04/23523

International filing date
(day/month/year) 22 July 2004 (22.07.2004)

Applicant
MERCK & CO., INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

S. Devi, Ph.D.

Telephone No. (571) 272-1600

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PCT 21569Y	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/23523	International filing date (<i>day/month/year</i>) 22 July 2004 (22.07.2004)	(Earliest) Priority Date (<i>day/month/year</i>) 24 July 2003 (24.07.2003)
Applicant MERCK & CO., INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of:



the international application in the language in which it was filed.



a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23523

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23523

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-9

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23523

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 39/02(2006.01),39/09(2006.01),39/00(2006.01);C07K 1/00(2006.01),2/00(2006.01);A01N 37/18(2006.01)

USPC: 530/350,300,825;514/2;424/190.1,234.1,237.1,184.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350, 300, 825; 514/2; 424/190.1, 234.1, 237.1, 184.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 200259148 A2 (CISTEM BIOTECHNOLOGIES GMBH) 01 August 2002 (01.08.2002), entire document especially Example 7 and page 220.	1-5 and 7-9
X	TAYLOR J.M. et al. Transferrin binding in Staphylococcus aureus: involvement of a cell wall-anchored protein. Mol. Microbiol. 2002, Vol. 43, No. 6, pages 1603-1614, especially Experimental procedures, Results, and Figure 3.	1-5 and 7-9

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
28 July 2006 (28.07.2006)

Date of mailing of the international search report

20 SEP 2006

Name and mailing address of the ISA/US
Mail Stop PCT. Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

S. Devi, Ph.D.

Telephone No. (571) 272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23523

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-9, drawn to a polypeptide immunogen comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1 without amino acids 609-645 of SEQ ID NO: 2.

Group II, claims 10-17 and 27-28 (in part), drawn to a nucleic acid comprising a recombinant gene comprising a nucleotide sequence encoding the polypeptide of Group I and a cell comprising the same.

Group III, claims 18, 19 and 29-32 (in part), drawn to a method of making a *S. aureus* polypeptide using a recombinant cell comprising the gene.

Group IV, claims 20-26, drawn to a method of inducing a protective immune response in a patient comprising administering the polypeptide of Group I.

Group V, claims 27-32 (in part), drawn to a yeast optimized nucleic acid sequence encoding an ORF0657n-related polypeptide and a method of making the polypeptide using the same.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of invention I is a polypeptide immunogen comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1 without amino acids 609-645 of SEQ ID NO: 2. This special technical feature is however already disclosed in the prior art. For example, CISTEM BIOTECHNOLOGIES GMBH (WO 200259148 A2) disclosed a polypeptide comprising an amino acid sequence lacking amino acids 609-645 of SEQ ID NO: 2 which is at least 90% identical to SEQ ID NO: 1. See the amino acid sequence with the accession number ABJ19106 of WO 200259148 A2 and the enclosed sequence alignment report. Therefore, the special technical feature does not define over the prior art and accordingly is not a unifying feature. The special technical features of the rest of the inventions are delineated above. The nucleic acid products of inventions II and V do not share significant structural elements with the polypeptide of invention I or with each other. Although the product of claim I and the method of using or making the same is a permitted combination under PCT Rule 13.2, in the instant case, since the product is already disclosed in the art, the special technical feature does not define over the prior art. Technically, the absence of special technical feature permits the separation of the methods of using or making the product from the product itself.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23523

Continuation of B. FIELDS SEARCHED Item 3:
WEST, DIALOG, MEDLINE, EMBASE, BIOSIS, Sequence databases
SEQ ID NO: 1-3, 7, 17, 20, and 42; inventors' names

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
MERCK & CO., INC.
126 EAST LINCOLN AVENUE
RAHWAY, NJ 07065-0907

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

20 SEP 2006

Applicant's or agent's file reference

PCT 21569Y

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/23523

International filing date (day/month/year)

22 July 2004 (22.07.2004)

Priority date (day/month/year)

24 July 2003 (24.07.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC: Please See Continuation Sheet

USPC: 530/350,300,825;424/190.1,234.1,184.1;514/2

Applicant

MERCK & CO., INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

28 July 2006 (28.07.2006)

Authorized officer

S. Devi, Ph.D.

Telephone No. (571) 272-1600

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/23523

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
☒ table(s) related to the sequence listing

b. format of material

- ☒ on paper
☒ in electronic form

c. time of filing/furnishing

- ☒ contained in the international application as filed.
☒ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/23523

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report(Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-9

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/23523

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>6</u>	YES
	Claims <u>1-5 and 7-9</u>	NO
Inventive step (IS)	Claims <u>6</u>	YES
	Claims <u>1-5 and 7-9</u>	NO
Industrial applicability (IA)	Claims <u>1-9</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-5 and 7-9 lack novelty under PCT Article 33(2) as being anticipated by Taylor *et al.*

It is noted that the claimed polypeptide immunogen is not required to be isolated. The claim uses the open claim language 'comprising'. The recited 'one or more additional polypeptide regions' being not provided as a carboxyl terminus as recited in claim 1 are not associated with the recited SEQ ID NO: 1.

Taylor *et al.* taught *S. aureus* cell wall fractions and cell wall proteins contained in a buffer comprising a transferrin binding polypeptide immunogen. The polypeptide comprises or consists essentially of an amino acid sequence that is 94.9% identical to SEQ ID NO: 1, 94.3% identical to SEQ ID NO: 3, and 94.8% identical to SEQ ID NO: 42. See attached sequence search reports. The *S. aureus* cell wall fractions are expected to contain other non-transferrin binding polypeptides or polypeptide regions inherently lacking a carboxyl terminus containing amino acids 609-645 of SEQ ID NO: 2, and an intrinsic adjuvant such as peptidoglycan.

Claim 6 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed polypeptide consisting of the recited amino acid sequences.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/23523

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 7 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 7 is indefinite for the following reason(s): Claim 7 is indefinite and confusing in the limitations 'immunogen comprising' and 'immunogen consists of', because it is unclear whether open ended or closed claim language is intended.

Claims 1-5 and 7-9 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: the instant specification does not provide the precise structure of the at least 94% or 90% identical polypeptide variants claimed which concurrently have the capacity to provide protective immunity against *S. aureus*. Obtaining such polypeptide variants that concurrently have the recited functional characteristics is not predictable and required undue experimentation in view of lack of specific disclosure and guidance.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/23523

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of IPC:

A61K 39/02(2006.01),39/09(2006.01),39/00(2006.01);C07K 1/00(2006.01),2/00(2006.01);A01N 37/18(2006.01)